

CLAIMS

1. A viral DNA construct encoding for a parvovirus that is capable of replication in a human or animal tumour cell comprising one or more selected transcription factor binding sites operatively positioned such as to promote expression of open reading frames encoding non-structural viral proteins, wherein the selected transcription factor binding sites are for a transcription factor the level or activity of which is increased in a human or animal tumour cell relative to that of a normal human or animal cell of the same type.
2. A viral DNA construct according to claim 1 wherein the transcription factor binding sites are positioned within the P4 promoter region.
3. A viral DNA construct according to claim 1 or claim 2 comprising a nucleic acid sequence corresponding to that of a wild type parvovirus wherein part of the wild type P4 promoter region is replaced by the one or more selected transcription factor binding sites.
4. A viral DNA construct as claimed in any one of the preceding claims characterised in that the wild type E2F enhancer is deleted.
5. A viral DNA construct as claimed in any one of the preceding claims characterised in that the selected transcription factor binding sites are for a transcription factor whose activity or level is specifically increased by causal oncogenic mutations.
6. A viral DNA construct as claimed in any one of the preceding claims characterised in that the selected transcription factor binding site is selectively activated in tumour cells containing oncogenic APC and β -catenin mutations.
7. A viral DNA construct as claimed in any one of the preceding claims characterised in that the selected transcription factor binding sites are single or multiples of a Tcf binding site sequence.

8. A viral DNA construct as claimed in any one of the preceding claims wherein the selected transcription factor binding site is a Tcf binding site sequence in the reverse orientation.
- 5 9. A viral DNA construct as claimed in any one of the preceding claims comprising a mutation which destabilises the capsid such as to reduce viral persistence in the environment.
- 10 10. A virus comprising or encoded by a viral DNA construct as claimed in any one of Claims 1 to 9.
11. A viral DNA construct, or a virus, as claimed in any one of Claims 1 to 10 for use in therapy.
- 15 12. A viral DNA construct, or a virus, as claimed in Claims 10 or Claim 11 characterised in that the therapy is of patients having neoplasms.
13. A viral construct, as claimed in any one of the preceding claims characterised in that it is capable of causing death of the tumour cell.
- 20 14. A viral DNA construct or a virus, as claimed in any one of the preceding claims wherein viral replication is reduced in normal cells compared with wild type virus.
- 25 15. A viral DNA construct or a virus, as claimed in any one of the preceding claims characterised in that viral replication is enhanced in cancer cells compared with replication of wild type virus in cancer cells.
- 30 16. Use of a viral construct, or a virus, as claimed in any one of the preceding claims in the manufacture of a medicament for the treatment of neoplasms.
17. A composition comprising a viral construct, or a virus, as claimed in any one of the preceding claims together with a physiologically acceptable carrier.

18. A composition as claimed in Claim 17 characterised in that it is sterile and pyrogen free with the exception of the presence of the viral construct or virus encoded thereby.
- 5 19. A composition as claimed in Claim 17 or Claim 18 characterised in that the carrier is a physiologically acceptable saline.
- 10 20. A method of manufacture of a viral DNA construct or a virus encoded thereby as claimed in any one of Claims 1 to 16 characterised in that it comprises transforming a viral genome having one or more wild type transcription factor binding sites controlling transcription of non-structural open reading frames, such as to replace one or more of these by tumour specific transcription factor binding sites.
- 15 21. A method as claimed in Claim 19 characterised in that the modified genome is transferred to a prokaryote for production of viral construct DNA.
- 20 22. A method of manufacture of a virus characterised in that viral construct DNA produced by a method as claimed in any one of Claims 20 to 21, is transferred to a mammalian cell for production of virus.
- 25 23. A method for treating a patient in need of therapy for a neoplasm wherein a viral DNA construct or virus as claimed in any one of Claims 1 to 15 is caused to infect tissues of the patient, including or restricted to those of the neoplasm, and allowed to replicate such that neoplasm cells are caused to be killed.
24. A method as claimed in Claim 23 characterised in that the patient is in need of therapy for a colon cell derived tumour.
- 30 25. A method as claimed in Claim 24 characterised in that the colon cell derived tumour is a metastasis located in the liver of the patient.